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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,960	05/02/2001	Susan E. Swift	A-69332-1/RMS/JJD	6153

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EXAMINER
CELSA, BENNETT M

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 03/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/847,960	SWIFT ET AL.	
	Examiner	Art Unit	
	Bennett Celsa	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14 and 17-34* is/are pending in the application.

4a) Of the above claim(s) *24-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12,17-23 and 27* is/are rejected.

7)☒ Claim(s) *13,14 and 28-34* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

Applicant's amendment dated December 24, 2003 is acknowledged.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of the Claims

Claims 1-14 and 17-34 are currently pending.

Claims 24-26 are withdrawn from consideration as being directed to a nonelected invention.

Claims 1-14, 17-23 and 27-34 are under consideration.

NOTE: APPLICANT'S CLAIMS AS PRESENTED IN THIS AMENDMENT SHOULD BE UPDATED TO DEPICT LATER AMENDMENTS TO THE ORIGINAL CLAIMS WHICH INSERTED SEQ. ID'S.

Allowable Subject Matter

Claims 13-14 and 28-34 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The following is an examiner's statement of reasons for allowance: the prior art of record fails to disclose or suggest the use of the specifically claimed probe sequences found in claims 13-14 and 28-34.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Withdrawn Objection (s) and/or Rejection (s)

In light of applicant's argument, the objection to the disclosure regarding Fig. 8 presented in the last office action, is hereby withdrawn.

In light of applicant's argument, the indefinite (or written description) rejection directed to the phrase "substantial complementary" is hereby withdrawn.

In light of applicant's amendment and argument, the written description rejection regarding labeling is hereby withdrawn.

In light of applicant's argument the new matter rejection of the phrase "from an immunoglobulin heavy chain gene locus" is hereby withdrawn.

In view of applicant's amendment and argument, the enablement rejection (e.g. addressing " a library of candidate agents") is hereby withdrawn.

New Objection (s) and/or Rejection (s)

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 9, 18-23 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Berton et al. PNAS USA Vol. 86 (April 1989) pages 2829-33.

Berton et al. teach a method for determining whether a candidate agent is capable of modulating germ line transcription (e.g. of IgG1) by:
adding a "candidate agent" (e.g. interleukin 4 or interferon gamma as "small peptide molecules") to a "plurality of cells" (e.g. lipopolysaccharide-stimulated B cells) using an "RNAse protection assay" e.g. antisense probes to mRNA from the immunoglobulin

heavy chain gene locus of IgG1 and quantifying the amount of germline mRNA to a control after the addition of RNAse See. E.g. Abstract; pages 2829-2830; Figures 1-4. It is noted that the means of producing the "candidate agent" (e.g. present claims 20-23) is not given patentable weight since the claim limitations amount to claiming the use of a product (e.g. candidate agent) by its means of manufacture (e.g. product by process). The reference disclosure of the produced probes (e.g. see the figures) indicates the production of clones containing less than 5 base mismatches.

Claims 1-2, 8-12, 17-23 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berton et al. PNAS USA Vol. 86 (April 1989) pages 2829-33.

Berton et al. teach a method for determining whether a candidate agent is capable of modulating germline transcription (e.g. of IgG1) by:

adding a "candidate agent" (e.g. interleukin 4 or interferon gamma as "small peptide molecules") to a "plurality of cells" (e.g. lipopolysaccharide-stimulated B cells) using an "RNAse protection assay" e.g. antisense probes to mRNA from the immunoglobulin heavy chain gene locus of IgG1 and quantifying the amount of germline mRNA to a control after the addition of RNAse See. E.g. Abstract; pages 2829-2830; figures 1-4. It is noted that the means of producing the "candidate agent" (e.g. present claims 20-23) is not given patentable weight since the claim limitations amount to claiming the use of a product (e.g. candidate agent) by its means of manufacture (e.g. product by process). The reference disclosure of the produced probes (e.g. see the figures) indicates the production of such clones as containing less than 5 base mismatches.

The Berton et al. reference method differs from the presently claimed invention by failing to additionally exemplify the utilization of the RNAse protection assay (with a second or greater different probes) to screen the ability of interleukin 4 or interferon gamma on other immunoglobulin IgG isotypes (E.g. IgG2-4) or IgE. See present claims 8 (IgE), claims 10-12 (IgG2-4) and claim 17 ("second RNAse probe").

However, the Berton et al. reference specifically teaches that Tcell-derived lymphokines (e.g IL-4 and/or interferon gamma) are known to play an important role in the regulation (e.g. induction/suppression of expression) of immunoglobulin isotype switching with regard to all of the IgG isotype species (e.g. IgG1-G4) as well as IgE (e.g. see page 2829, especially left column) and abstract.

Accordingly, one of ordinary skill in the art would be motivated to further apply the Berton et al. reference method utilizing an RNAse protection assay (including making the corresponding antisense probes) as it applies to the Tcell derived lymphokines (e.g. IL-4 and/or interferon gamma) in order to evaluate the effect of these cytokines on isotype switching as it relates to IG2-4 or IGE.

Thus, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to utilize the Berton reference RNAse protection assay (with a second or greater different probes) to screen the ability of interleukin 4 or interferon gamma on other immunoglobulin IgG isotypes (E.g. IgG2-4) or IgE.

Claims 1-3, 5-12, 17-23 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berton et al. PNAS USA Vol. 86 (April 1989) pages 2829-33 and Turaga et al. J. Immunol. Vol. 151 (3) (Aug. 1993) pages 1383-1390.

Berton et al. teach a method for determining whether a candidate agent is capable of modulating germ line transcription (e.g. of IgG1) by:

adding a "candidate agent" (e.g. interleukin 4 or interferon gamma as "small peptide molecules") to a "plurality of cells" (e.g. lipopolysaccharide-stimulated B cells) using an "RNAse protection assay" e.g. antisense probes to mRNA from the immunoglobulin heavy chain gene locus of IgG1 and quantifying the amount of germ line mRNA to a control after the addition of RNAse See. Eg. Abstract; pages 2829-2830; Figures 1-4.

It is noted that the means of producing the "candidate agent" (e.g. present claims 20-23) is not given patentable weight since the claim limitations amount to claiming the use of a product (e.g. candidate agent) by its means of manufacture (e.g. product by process). The reference disclosure of the produced probes (e.g. see the figures) indicates the production of such clones as containing less than 5 base mismatches.

The Berton et al. reference method differs from the presently claimed invention by failing to:

a. additionally exemplify the utilization of the RNAse protection assay (with a second or greater different probes: see claim 17) to screen the ability of interleukin 4 or interferon gamma on other immunoglobulin IgG isotypes (E.g. IgG2-4: claims 10-12), IgA (claims 6-7) or IgE (claim 8);

and

b. teach a labeled (e.g. radio isotopic) probe (e.g. claims 3 and 5).

Regarding item a. above, the Berton et al. reference specifically teaches that Tcell-derived lymphokines (e.g. IL-4 and/or interferon gamma) are known to play an important role in the regulation (e.g. induction/suppression of expression) of immunoglobulin isotype switching with regard to all of the IgG isotype species (e.g. IgG1-G4) as well as IgE (e.g. see page 2829, especially left column) and abstract. Additionally, Turaga et al. teach that "[T]ransforming growth factor beta selectively induces IgA." (see Turaga et al. page 1383, left column).

Accordingly, one of ordinary skill in the art would be motivated to further apply the Berton et al. reference method utilizing an RNAse protection assay (including making the corresponding antisense probes) as it applies to the Tcell derived lymphokines (e.g. IL-4 and/or interferon gamma and/or transforming growth factor) in order to evaluate the effect of these cytokines on isotype switching as it relates to IgG2-4, IgA or IgE.

Thus, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to utilize the Berton reference RNAse protection assay (with a second or greater different probes) to screen the isotype switching ability of various lymphokines on other immunoglobulin species including IgG isotypes (E.g. IgG2-4); IgE or IgA.

With regard to item B. above, it is further noted that Turaga et al. (e.g. see abstract; pages 1384/1386 and figures) utilizes radioisotopic labeling (e.g. S32 or P32) of antisense RNA probes in the same assay methods as utilized in the Berton et al.

reference method thus rendering the use of such radioisotopic labeling in the Berton et al. method prima facie obvious to one of ordinary skill in the art at the time of applicant's invention.

Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Berton et al. and Turaga et al. as applied to claims 1-3, 5-12, 17-23 and 27 above, and further in view of Chan et al. Analytical Biochemistry Vol. 242 (1996) pages 214-20.

The Berton et al. and Turaga et al. references teach the use of methods for determining whether a candidate agent is capable of modulating transcription of various germ line immunoglobulin heavy chain gene loci using RNAse protection assays utilizing unlabeled and radioisotopically labeled antisense RNAse protection probes but differ from the presently claimed invention (e.g. claim 4) by failing to utilize fluorescent labeled antisense RNAse protection probes. See above discussion of The Berton et al. And Turaga et al incorporated by reference in its entirety.

However, Chan et al. teach a nonisotopic RNAse protection assay utilizing fluorescent probes which advantageously avoids/minimizes radioisotope use.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to utilize fluorescence probe labels in the Berton et al. and Turaga et al. RNAse protection assays as taught by Chan in order to avoid/minimize radioisotope use.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Future Correspondences

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bennett Celsa whose telephone number is 571-272-0807. The examiner can normally be reached on 8-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-273-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bennett Celsa
Primary Examiner
Art Unit 1639

BC
March 15, 2004